UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

ASTELLAS INSTITUTE FOR REGENERATIVE MEDICINE,

Plaintiff,

v.

IMSTEM BIOTECHNOLOGY, INC., XIAOFANG WANG, and REN-HE XU,

Defendants.

C.A. NO. 1:17-cv-12239-ADB

Leave to File Granted on 5/27/21

ASTELLAS' REPLY IN SUPPORT OF ITS MOTION FOR ENTRY OF PROPOSED JUDGMENT

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Abbreviation	Term
’956 patent	U.S. Patent No. 8,961,956
’321 patent	U.S. Patent No. 8,962,321
’551 patent	U.S. Patent No. 9,745,551
’122 patent	U.S. Patent No. 10,557,122, (Subject to stipulation, *see* ECF No. 255 at 38 n.17)
’944 application	U.S. Patent Application No. 16/745,944 (Currently pending application with same disclosure as the ’551 patent)
Astellas	Astellas Institute for Regenerative Medicine
EBs	Embryoid Bodies
ESCs	Embryonic Stem Cells
HB	Hemangioblast
HB-MSC	Hemangioblast-derived Mesenchymal Stem Cell
hESCs	Human Embryonic Stem Cells
ImStem	ImStem Biotechnology, Inc.
MS	Multiple Sclerosis
MSCs	Mesenchymal Stem Cells
Opp.	Defendants’ Opposition to Astellas’ Motion for Entry of Proposed Judgment and for Additional Findings and Conclusions Concerning Massachusetts General Laws, Chapter 93A [ECF No. 265]
Patent Office	U.S. Patent & Trademark Office
PCT	Patent Cooperation Treaty (a type of international patent application)
’551 PCT Application	Defendants’ PCT Application No. PCT/US2013/048291 [*See* ECF No. 247-1 at ¶ 134 (defining same)]

All emphasis added unless otherwise noted.

I. INTRODUCTION

From its original complaint, Astellas put Defendants on notice that it was seeking return of the HB-MSC patent portfolio Defendants improperly filed for and obtained on Astellas' HB-MSC technology. Defendants pressed the issue further by alleging that they were inventors on Astellas' own patents, a theory the Court rejected after hearing extensive evidence on the state of the art and work each group of scientists had done. Moreover, Astellas' experts offered opinions that nothing in the disclosure in the '551 patent, was an inventive contribution of Drs. Wang or Xu. And despite now suggesting that it was never litigated, Defendants repeatedly told the Court that '551 PCT Application was identical to the '551 patent. Astellas' proposed final judgment comports with what it sought from the beginning—return of the HB-MSC patent portfolio Defendants wrongfully filed on Astellas' HB-MSC technology.

II. DEFENDANTS SHOULD BE ORDERED TO COOPERATE TO TRANSFER OWNERSHIP OF THE '551 AND '122 PATENTS

The Court should order Defendants to cooperate with Astellas to transfer ownership of the '551 and '122 patents. Defendants do not dispute that 1) the final judgment should include an order to correct inventorship on the '551 and '122 patents (Opp. 3), or that 2) once inventorship is corrected and because ownership flows from inventorship, Astellas is the sole owner of these patents (Opp. 3-4). Yet, Defendants oppose having to cooperate with Astellas to effectuate the transfer of ownership, offering no justification for their opposition except to contend it is "unnecessary." Opp. 3-4. This is not appropriate and itself suggests that Defendants may be unwilling to do any required paperwork to transfer ownership of these patents, rending the Court's ordering them to do so necessary.

III. ASTELLAS HAS SOUGHT RETURN OF THE ENTIRE PATENT PORTFOLIO THROUGHOUT THIS LITIGATION

Despite Defendants protestations (Opp. 4-10), Astellas provided notice that the entire HB-

MSC patent portfolio Defendants improperly filed for and obtained on Astellas' HB-MSC technology has been at issue since the beginning of this case. Astellas explained in its original complaint the patent applications that Defendants filed that contained Astellas' HB-MSC technology include the '551 PCT Application. Compl. ¶ 47, ECF No. 1; Amend. Compl.¶ 47, ECF No. 113. As Defendants grudgingly concede, Astellas requested an order transferring and/or granting a constructive trust for Astellas over the '551 PCT Application and any other applications deriving from Defendants' false claims of inventorship in its original complaint. *See* Opp. 15; Compl. ¶ 86(E), (F), ECF No. 1; Amend. Compl. ¶ 92(E), (F), ECF No. 113.

Further, in their opening reports, Astellas' experts, Drs. Fortier and Brivanlou, walked through the entire disclosure (examples, figures, claims) of the '551 patent, which Defendants told the Court was identical to that of the '551 PCT Application in both their pre- and post-trial filings (*see, e.g.*, ECF No. 221 at ¶ 62 n.9; ECF No. 247-1 at ¶ 134), and explained how Defendants did not contribute anything inventive to that disclosure. *See* ECF No. 199-21 at ¶¶ 96-149; ECF No. 199-22 at ¶¶ 199-271; ECF No. 199-23 at ¶¶ 32-39. Defendants had an opportunity to respond in their rebuttal expert reports, and raise or try to rebut Drs. Fortier's and Brivanlou's opinions. Yet, Defendants chose not to raise any other alleged contributions from Drs. Wang or Xu other than those addressed at trial. *See, e.g.,* ECF No. 199-25 at ¶¶ 2, 10, 23; ECF No. 199-26 at ¶¶ 3, 18, 32; *see also* ECF No. 199-24 at ¶¶ 17, 30, 65-89.

Defendants specifically acknowledged that Astellas was seeking return of the '551 PCT Application prior to trial, writing in their pretrial memorandum that Astellas "***contend[s] that Wang and Xu claimed Plaintiff's (alleged) technology as their own*** by seeking patent protection for a method for producing human embryonic stem cell-derived mesenchymal stem cells from a hemangioblast intermediary ***in the '551 PCT Application***." ECF No. 221 at ¶ 138. Astellas' own

pretrial brief expressly stated "Astellas should also be granted equitable relief in the form of ***return [of] all intellectual property rights that contain its MSC technology, including all patents and applications Defendants have filed, worldwide, that contain Astellas' MSC technology.***" ECF No. 219 ¶ 256; *see also id.* ¶¶ 294, 297, 326. So there is no reasonable debate that Defendants were on notice that Astellas was seeking return of all of its intellectual property.

Yet, now having lost on inventorship, Defendants argue the exact opposite—that Astellas "never previously mentioned" that it would seek a final judgment on inventorship of the '551 PCT Application and related applications and patents. Opp. 5. In so doing, Defendants also reverse position on one of their own post-trial proposed findings of fact, where they sought this Court to find that "[t]he '551 PCT Application was the basis for the '551 national stage and thus has the same specification and figures as the '551 patent." ECF No. 247-1 at ¶ 134. Now, Defendants argue that ***Astellas*** took an "(incorrect) approach of assuming that all of these patents and applications are identical." Opp. 9. Once again, as Astellas has pointed out when Defendants deployed such turnabout tactics at summary judgment and in their motions *in limine*, "the Court certainly should not countenance Defendants' strategy of telling the Court one thing to convince it to rule in their favor, then arguing that that statement cannot be used at all when it no longer suits their purposes." ECF No. 155 at 5; ECF No. 198 at 2 n.2.

Regardless, Defendants' examples purporting to show the '551 PCT Application and its related applications and patents present factual disputes not already decided by this Court show no such thing.[1] First, Defendants admit that claims of the foreign patents and applications "are very

[1] Defendants cite numerous cases for the non-controversial points that inventorship is determined with reference to the claimed subject matter, that contribution to one claim is sufficient for one to be an inventor, that an inventor's contribution must not be insignificant in quality when measured against the full scope of the invention, and that inventorship need be proven by clear and convincing evidence. *See* Opp. 4-10. Those cases have nothing to do with the issue here.

similar to" or "overlap with those in the '551 and '122" patents, which Defendants do not dispute were addressed in the Court's decision. Opp. 7 n.3.

Second, Defendants mischaracterize their selected examples. Claims 27-58 of the '551 PCT Application do not, as Defendants assert, relate to therapeutic use of MSCs for "various diseases" that "w[ere] not considered by this Court in rendering its inventorship decision." Opp. 6-7. The "various diseases" in these claims are therapeutic use of MSCs for autoimmune disease (claims 27-42, TX-8 at AIRM293606-08) and for MS (claims 43-58, TX-8 at AIRM293608-10). Both were expressly addressed at trial. Further, the Court expressly addressed these diseases in its opinion, holding that the "evidence presented at trial demonstrates that ***using MSCs to treat autoimmune diseases, including MS***, was already being done in the field and was known to Drs. Kimbrel, Lanza, Wang, and Xu prior to the collaboration" and that "***Dr. Lanza had the idea to use HB-MSCs to treat autoimmune diseases, including MS***, prior to the collaboration." ECF No. 255 at 19. Far from being "additional subject matter that the Court never considered in rendering its inventorship decision" as Defendants contend (Opp. 6), the Court squarely considered and resolved these issues in holding against Defendants on the inventorship claims.

Defendants' argument that the claims in the '944 application[2] somehow raise different factual issues that require further litigation because they "claim methods of producing embryoid bodies and hemangioblasts" and not methods for producing HB-MSCs or are "directed to never-

[2] Defendants' cited cases regarding correction of inventorship of applications under 35 U.S.C. § 116 are inapposite. *See* Opp. 15-16. All those cases addressed inventorship claims based *only* on patent applications. That is not the case here, where Astellas' correction of inventorship claim under 35 U.S.C. § 256 involved an issued patent (i.e., the '551 patent), the parties actually litigated whether Defendants contributed anything to the entire disclosure of the '551 patent (and Defendants lost), the '944 application has the exact same disclosure as the litigated '551 patent, and the pending dispute is over whether the relief awarded to Astellas under the Court's '551 patent inventorship determination should also include correction and transfer of ownership of the '944 application to Astellas. It should. To hold otherwise would elevate form over substance.

contested claims" (Opp. 7-8, 18) similarly fails. Defendants omit that, as was extensively discussed at trial, the method of making embryoid bodies from ESCs in the '944 application claims is the ***first and second steps*** in the method of making HB-MSCs and the method of making hemangioblasts is the ***first through third steps*** in the method of making HB-MSCs that the parties litigated. *Compare* Ex. A[3] at 5 *with* '551 patent claim 1. After considering all the evidence, the Court found that Drs. Wang and Xu's alleged contributions to these steps merely followed the teachings in Dr. Brivanlou's articles, published years earlier, and Drs. Wang and Xu should be removed as inventors. ECF No. 255 at 24-27, 42-44. Again, far from presenting new factual disputes, the Court's decision considered and resolved any factual issues in the '944 application claims.

In short, throughout this litigation, Astellas repeatedly notified Defendants that it was seeking return of all patents and applications Defendants filed on Astellas' HB-MSC technology. This includes the '551 PCT Application and the related applications and patents that Astellas included in its proposed final judgment. Further, Defendants' contention that these applications potentially present new factual issues not yet resolved by the Court fails because the Court did, in fact, address these issues explicitly in its decision.

IV. THE COURT CAN ORDER TRANSFER OF THE '551 PCT APPLICATION AND RELATED PATENTS AND APPLICATIONS

As Astellas explained, the Federal Circuit has held that, having determined inventorship of the underlying U.S. patent, the Court can "instruct [Defendants] to take appropriate action to change the inventorship designation on the foreign patent applications," as "inventorship on such

[3] The Court may take judicial notice of this filing, even after the close of evidence, as it is publicly available on the Patent Office's Public PAIR database, https://portal.uspto.gov/pair/PublicPair. *See, e.g.*, *Group One, Ltd. v. Hallmark Cards, Inc.,* 407 F.3d 1297, 1306 (Fed. Cir. 2005) (district court permissibly took judicial notice of patent's reinstatement, which was evident from Patent Office filings that occurred after close of the evidence, under Fed. R. Evid. 201(f)).

applications normally follows the inventorship designation in the originating country." *Chou v. Univ. of Chicago*, 254 F.3d 1347, 1360 (Fed. Cir. 2001). *Chou* is controlling law and Defendants attempts to distinguish it all fail. Defendants argue that *Chou* is distinguishable because it involved "PCT applications that were filed in the U.S. States [sic] Patent and Trademark Office" and that the "PCT applicants had also elected the United States as the Contracting State in which they intended to pursue national patent rights." Opp. 13. Defendants omit, however, that Defendants also filed their PCT Application at issue in this case with the United States Patent and Trademark Office, which is readily apparent from the PCT Application number itself: PCT/**US**2013/048291. *See also* Ex. B[4] ("Transmittal Letter To The United States Receiving Office" for the '551 PCT Application and Receipt identifying the "Application Type" as "International Application for filing in the US receiving office"). Second, Defendants, as in *Chou*, elected the United States as where they intended to pursue—and did pursue—national patent rights, *i.e.* the '551 patent. Thus, neither of these points actually distinguish *Chou*.

Finally, *Chou*'s language is not dicta or "moot" as Defendants argue. Opp. 13-14 & n.5. The Federal Circuit reversed the district court's decision that Dr. Chou lacked standing to sue to correct inventorship of U.S. patents and explained that, as a result, "we need not determine if she is a proper declaratory plaintiff in an action to correct inventorship on those [PCT applications] under the Declaratory Judgment Act; ***such a decision would not afford her any relief that is not also available through the § 256 action***." *Chou*, 254 F.3d at 1360. In other words, the Federal Circuit recognized that Dr. Chou could get the relief she sought—correction of the PCT applications (and, as discussed above, the related patents and applications)—through her § 256 action, without need for a separate declaratory judgment claim specific to the PCT applications.

[4] The Court may take judicial notice of this filing, for the same reasons in *supra* n.3.

That is exactly Astellas' point and exactly what it proposes the judgment include. In the face of the Federal Circuit's precedential *Chou* decision, Defendants cite only a single-sentence footnote from a non-precedential decision.[5] Opp. 10 (quoting *Kamdem-Ouaffo v. PepsiCo Inc.*, 657 F. App'x 949, 953 n.5 (Fed. Cir. 2016)).[6] Defendants also omit the case citation included in that footnote, *Voda v. Cordis Corp.*, which does not address inventorship at all, but rather whether district courts may "exercise jurisdiction over ***infringement claims based on foreign patents***." 476 F.3d 887, 900 (Fed. Cir. 2007). Simply put, *Chou* controls and this Court can and should order Defendants to cooperate with Astellas to transfer ownership of the '551 PCT Application and related foreign patents and applications to Astellas.

Should the Court prefer, it can, however, order the equitable relief of returning all the patents and applications Defendants filed on Astellas' HB-MSC technology under Astellas' Chapter 93A claim. Section 11 of Chapter 93A expressly allows the Court to order "such equitable relief, including an injunction, as the court deems to be necessary and proper." Mass. Gen. L. Ch. 93A, § 11; *see Kattar v. Demoulas*, 433 Mass. 1, 17 (2000) ("[Chapter] 93A provides the possibility for broad, far-reaching equitable relief").

Defendants do not dispute that the Court has the power to and can order such equitable relief. Instead, Defendants raise other arguments against this route, all of which fail. First,

[5] Defendants cite the PCT Applicant's Guide, which is not controlling on this Court, for their assertion that "the laws of inventorship are different in different countries." Opp. 11. Defendants omit that that section of the Guide continues on to state "[w]here, ***and this is the usual case, all the inventors are the same for all designated states***, no special indication" is required on the request form for the application. PCT Applicant's Guide § 5.038. Moreover, Defendants did not indicate that the inventors would be different in different countries for the '551 PCT Application, as is evident from their request form, which does not check the box for "Further Applicant(s) and/or (Further) Inventor(s)" as the Guide instructs. Ex. B at 2.

[6] Defendants' other cases stand for the non-objectionable point that U.S. patent laws do not apply extraterritorially, which is not relevant to the issue here. *See* Opp. 10.

Defendants try to resurrect their argument that Astellas' Chapter 93A claim is preempted by federal patent law. Opp. 16-17. Defendants' preemption argument is substantively meritless for the reasons Astellas has previously explained. *See* ECF No. 227 at 5 n.5. Defendants are also barred from raising it, as it is an affirmative defense that must be pled and Defendants did not raise it until their pre-trial memorandum, despite having considered whether to raise it for the prior eight months. *See* ECF No. 227 at 1 & n.2; 2020.08.12 Hr'g Tr. 15:7-16; 2020.08.26 Hr'g Tr. 3:18-24. In fact, faced with authority provided by Astellas and the Court, Defendants ***withdrew*** their preemption defense rather than attempt to justify it in briefing. 2020.08.26 Hr'g Tr. 3:18-4:3 (Mr. Shannon stating "[w]e've already withdrawn that defense"); ECF No. 230 ("we are writing to advise the Court that preemption is no longer an issue that needs to be addressed by the Court").

Second, Defendants' assertion that the Court's decision rejected Astellas' Chapter 93A claim misunderstands Astellas' argument. As Astellas explained in its opening motion, Astellas respectfully requested the Court reconsider/extend its Chapter 93A conclusions of law "based on Defendants' post-trial activity—namely, ***refusing to return the related applications, despite the inventorship findings of this court***." ECF No. 262 at 8. After the Court's decision, Defendants have no credible claim to have contributed anything in the '551 patent disclosure (which, again, is the identical disclosure in the '551 PCT Application and related applications and patents). And Defendants can no longer claim to misunderstand the value of their contributions to the parties' collaboration, as the Court's decision clearly explained why those contributions were insufficient for inventorship. *See* ECF No. 255 at 46. Essentially, Defendants are, at this point, trying to hold on to intellectual property they sought covering Astellas' HB-MSC technology that they know, from this Court's decision, that they have no rights to. Not only is that unfair, it is egregiously so.

Third, Defendants' incorrectly state that, because neither party has a product on the market,

somehow Astellas cannot prove actual economic harm. *See* Opp. 18-19. Defendants argument assumes that, because there are no products on the market, the patents and applications at issue have no value. Of course that is not true. If it were, why would the parties have invested millions litigating inventorship and ownership of patents that have no value? Why would Defendants oppose returning the '551 PCT Application and related patents and applications to Astellas? Defendants' argument that the patents and applications have no value is not credible on its face. Regardless, both Astellas and Defendants indicated that they are continuing efforts to develop MSCs as therapies. However, these efforts take time to complete clinical trials and to receive regulatory approval.

Fourth, while the Court may need to address Defendants' statute of limitations and unclean hands defenses to Astellas' Chapter 93A claim should it choose to reconsider its conclusions of law, these defenses fail for the reasons Astellas described in its post-trial briefing. *See* ECF No. 243 ¶¶ 95-99; ECF No. 245 ¶¶ 14 & n.7, 15. Further, the Court should reject Defendants' argument, which the Court recognized Defendants raised for the first time in their post-trial briefing, "that they were not engaged in trade or commerce for the purposes of Chapter 93A liability," as belatedly raised. *See* ECF No. 255 at 44 n.20.

In short, should the Court so choose, it has the power to revisit its conclusions of law as to Astellas' Chapter 93A claim (pursuant to Federal Rules of Civil Procedure 52(b) and/or 59(a)(2)), and could order the equitable relief of returning the HB-MSC intellectual property that Defendants improperly took and now seek to retain.

V. THE COURT HAS POWER OVER DRS. WANG AND XU AND SHOULD ORDER THEM TO COOPERATE TO TRANSFER THE PATENTS AND APPLICATIONS

Finally, the Court should reject Defendants' argument, mentioned only in a footnote, that Defendants "do not own or control the Chinese patent." Opp. 7-8 n.3. Defendants' argument

misses the point—Astellas is asking the Court to order Drs. Wang and Xu (and ImStem, as appropriate) to cooperate in submitting the necessary paperwork to the Chinese, Hong Kong, and Canadian patent offices in order to transfer ownership of the relevant patents and applications to Astellas. There can be no dispute that the Court has power over Drs. Wang and Xu (and ImStem, as appropriate) to order them to do so. All Astellas seeks is a return of what this Court already decided that Drs. Wang and Xu had no rights to in the first place—all patents and applications Defendants have filed, worldwide, that contain Astellas' MSC technology. *See* ECF No. 219 ¶ 256; *see also id.* ¶¶ 294, 297, 326.

VI. CONCLUSION

For the above reasons, Astellas respectfully requests that the Court enter Astellas' proposed judgment, attached to its Motion as Exhibit A.

Dated: June 9, 2021

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that this document, which was filed with the Court through the CM/ECF system, will be sent electronically to all registered participants as identified on the Notice of Electronic Filing, and paper copies will be sent on June 9, 2021 to those identified as non-registered participants.

/s/ David P. Frazier
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